

Medical (Neurologic) Review

10/1/06

Case: Mark Fix

I have reviewed the medical records of Mr. Mark Fix from the Bureau of Prisons (McKeen, Loretto, and Rochester), the Mayo Clinic Minnesota, Joseph Joseph MD, J. Stephen Shymansky M.D., Altoona Hospital/Neurology/Laurence Primack, Bradford Regional Medical Center, and Seneca Eye Surgeons. I have reviewed MRI films as listed in this report. This review was performed in order to render an opinion regarding the etiology of neurologic (particularly) symptoms, whether the medical evidence documents if he has the condition Multiple Sclerosis (MS), and whether he has documentation of Lyme Disease (borreliosis).

Mr. Fix was born 9/28/1956 and was therefore 43 years old on 5/15/2000 when the issues related to this case began. He was incarcerated at the Federal Correctional Institute (McKean) at that time. Available medical records show a history of a motor vehicle accident with a hip fracture in 1999, tobacco use, and an episode of low back pain and left leg numbness in 1991.

He was seen at the FCI medical office on 5/15/00 for a recurring lip lesion that was diagnosed as an outbreak of herpes simplex viral infection (commonly known as a "cold sore") and also reported to the medical personnel "pt thinks he was bitten in the r (right) leg 3 days prior" (per the medical record recorded on that day). Mr. Fix described the area was red and itchy. Two small areas of erythema (redness) were noted on exam without swelling or discharge. These were felt to either be due to a spider bite or possibly allergic dermatitis. He was given treatment for the cold sore (Valtrex) and the skin lesions (hydrocortisone cream).

He returned to the medical office on 5/28 with a report of blurred vision in his left eye since 5/27. No pain or injury was noted. His eye exam was normal. He was to follow-up with the physician in the am. At the next morning's health clinic visit, he reported an inability to distinguish shapes and colors with that eye and also decreased depth perception. He was sent that day to the Bradford Regional Medical Center emergency room for evaluation on 5/29. He was seen by their physicians Dr. Breznik who did an appropriate history and exam, a blood test called a Sed Rate which was minimally and nonspecifically elevated, and a CAT Scan of the Brain and Orbits (eye region) which showed only sinus changes which were felt to all be unlikely to be related to his visual complaints. The ER physician documented that he discussed the patient's condition by phone with Dr. Keverline, an Ophthalmologist, and it was felt that this condition was possibly optic neuritis, macular edema, or less likely central retinal artery occlusion. The ophthalmologist requested the patient be treated with topical steroid eye drops as well as oral prednisone (also a steroid) 10 mg 2 pills twice per day and be referred in for evaluation that week. He was given the recommended treatment and was seen on 6/2 by ophthalmology who at that time diagnosed optic neuritis and discontinued the eye drops. The next ophthalmologic follow up on 6/8 confirmed the diagnosis of optic neuritis and requested additional tests including laboratory (blood) tests and a carotid doppler (ultrasound). These tests were ordered on 6/12 and the all blood tests were drawn on 6/20. Results of the blood tests were normal for the RPR, biochemistry profile,

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thyroid, and CBC except for high cholesterol. The screening blood test for Lyme was abnormal (positive) and therefore the lab did the more specific test (Western Blot) automatically. The negative Western Blot (WB) test result was completed and reported from the lab on 7/7 and noted by the medical staff on 7/10. As the WB is a better test, it takes longer to do than the screening test. Most labs and physicians will first do the screening test known as an ELISA or IFA and only proceed with the WB if the screen is positive. The confirmatory WB test was absolutely negative for both acute and chronic Lyme exposure/infection. Of a potential 10 bands on the IgG WB that may be seen with Lyme exposure (as early as 2 weeks after infection starts), Mr. Fix had zero bands. A positive IgG WB for Lyme requires multiple positive bands. Of the potential three bands seen on the IgM test (which is positive within days of new infection), none were present. A positive IgM WB requires 2 of the three bands to be present. The lab report itself emphasizes that both the IgM (acute) and IgG (chronic) bands should be present by this point (greater than 4 weeks from initial exposure) if a patient has been infected with Lyme. The negative test result was reported from the lab on 7/7 and initialed by the medical staff (Olson) on the chart on 7/10. At this point it can be definitively stated that Mr. Fix did not have Lyme Disease from an exposure occurring in mid-May of 2000. The cause of his optic neuritis remained idiopathic (unknown) and his vision remained severely impaired. His carotid artery doppler test was normal as well. He completed his prednisone treatment. Mr. Fix reported on a medical form (now he was at the FCI in Loretto) on 9/12 "I also have, what I do believe to be a tick bite" and that he had had the problem for 2-3 weeks. It is documented that he did not show up for his medical appointment on 9/18. He did not bring these issues up at his next medical appointment on 10/19 when he was seen for a cold for which he received the antibiotic Bactrim 1 pill 2 times per day for 10 days, hip pain for which he received ibuprofen, and another cold sore for which he was treated. His follow-up ophthalmology exam on 10/26 revealed atrophy or shrinkage of his left optic nerve, compatible with the severity of his optic neuritis that occurred in May. A follow up appointment was suggested in 6 months from the October appointment. All medical tests and follow-up appointments were completed as requested by Mr. Fix's treating medical personnel.

Mr. Fix next experienced right eye visual loss reported on 11/29. He was seen that day and referred to optometry and subsequently ophthalmology who both saw him on 11/30. He reported some discomfort in and over the right eye (noted in 1/3/01 summary note). No treatment was specifically recommended. Laboratory studies and an MRI of the brain and orbits were ordered. He later reported he had experienced a lesion on his penis this month and felt it was likely herpes as a previous partner had this condition. The labs included a CBC, Sed Rate, and RPR and were negative. The MRI was completed on 12/7 and revealed multiple lesions in a pattern entirely typical for MS. I have personally reviewed these films. They are so typical for MS in pattern, distribution, and inflammation that I could use them to teach my medical students and residents. Consultation with a Neurologist was recommended by Ophthalmology and ordered by the FCI medical staff. Ophthalmology reported that they did not want to see the patient back at this time. This is likely due to the fact that no treatments exist at this time that change the degree of recovery or repair when a person experiences optic neuritis. The presence of viral infections, namely the cold sore in May and the possible

genital herpes in December, are relevant as the most common trigger for MS attacks is viral infection.

Dr. Primack, a neurologist, saw the patient on 12/19. Dr. Primack reviewed his history, exam, and test results and noted the abnormal MRI report. Among other things he noted was the previous normal Lyme test. He informed Mr. Fix of the likely diagnosis of MS and lack of available treatments for his visual loss.

Mr. Fix had a doctor visit on 1/3/01 and was given Amoxicillin for sinus symptoms. Additional labs revealed elevated antibodies to Herpes Simplex with normal vitamin B12, folate, and angiotensin converting enzyme levels. Electrodiagnostic studies ordered by Dr. Primack did not suggest additional diagnoses and supported the prior diagnosis of optic neuritis in both eyes. I have reviewed the electrodiagnostic reports and agree with the interpretation. Dr. Primack saw the patient on 1/22/01 and commented, "If pt has Lyme, treat, if not treat for MS with Avonex." It is unclear to me why Dr. Primack's comments about Lyme arose on this date however a consultation with an Infectious Disease (ID) specialist was ordered that day. A mid-level practitioner saw the patient on 1/23 who reviewed his history and labs. Specific questions at this time did not disclose any secondary Lyme symptoms such as fever, fatigue, or joint pain. When specifically questioned about the rash of 5/00, the patient stated that he did not recall the classic rash appearance of a target with a clear area surrounded by redness (bull's eye or erythema migrans). As the appointment with ID was scheduled for 3/9/01, the Lyme blood test was repeated on 1/25. Consultations with Board Certified ID physicians are often difficult to get in western Pennsylvania and a 6-week wait is within the standard of care for this non-emergent case. This repeat Lyme lab result returned on 2/1 again showing a positive screening test (EIA) titer of 1.29 with positive being above 1.10. The WB IgG test was again negative, revealing only 1 band positive out of ten (at least 5 are required positive to diagnose Lyme). The screening EIA for the early infection was also positive at 1.44 (positive if >1.00) however again all 3 of 3 bands on the more accurate WB test were negative again. I personally reviewed the original lab report. There is no doubt this is a negative test. The format of the results pages is somewhat misleading as the results of the screening tests (which were positive) are in bold text, the results of the more accurate WB tests, which are negative, are not in bold. This convention (bold for abnormal results) is not meant to signify which test is more important but rather to draw physician's attention to a result. Dr. Leonard called Dr. Sullivan of ID with the preliminary positive screening test on 2/1 (before the WB negative results returned). Dr. Sullivan suggested antibiotic treatment with either intravenous Rocephin or oral Doxycycline pending the rest of the results and his actual consultation. Doxycycline was started 2/1. The FCI medical staff met all care standards by calling the ID physician for preliminary recommendations. When the WB results came back a 2/5 medical note states that treatment would continue until the ID consult was completed.

Mr. Fix experienced unsteadiness on his feet, a likely MS attack on 2/12. The negative results of the WB test were documented and the pending ID consult was awaited. His MS symptoms worsened with more numbness and fatigue by 2/15. He was able to walk about on his own. His neurologist was called. As the patient did not yet have his ID consult, Dr. Primack the neurologist continued to defer on starting Avonex, a long term therapy to help control MS. Referral to the Federal Medical Center was requested however Mr. Fix refused this. His neurologic symptoms fluctuated and his

vision showed some mild improvement. Dr. Sullivan of ID saw him for an initial visit on 3/9/01. Dr. Sullivan noted the prior treatment for 5 weeks with Doxycycline and noted, "could complete course with amoxicillin". It is not clear from available notes if Dr Sullivan thought this was a Lyme infection or not. He did order tests for other diagnoses, which came back negative. Amoxicillin was ordered for 18 days and Doxycycline was stopped. The ID physician did recommend a lumbar puncture (also known as a spinal tap). Mr. Fix continued to refuse transfer to the Federal Medical Center (FMC). He completed the antibiotics approximately 3/30. On 4/9 he experienced another MS attack with worsening balance and numbness. Dr. Primack was called. Mr. Fix finally agreed to transfer to the FMC in Rochester Minnesota on 4/11 and was accepted there on 4/18.

His evaluation at the FMC included general medical, neurologic, infectious disease, and ophthalmologic consultations, an MRI Brain Scan, and a lumbar puncture. Dr. Daube, the neurology consultant felt his prior MRI was not necessarily typical for MS but might suggest vascular disease (Vasculitis). I strongly disagree as I previously noted it was a textbook example of the MS. I note that while Dr. Daube is a neurologist, his area of sub-specialization is in epilepsy (seizures), not MS. I specialize in MS and treat over 1000 people with MS. I direct an MS Center. His new MRI Brain films of 5/25 were also personally reviewed and show changes typical for MS with new lesions in the brainstem (medulla), left middle cerebellar peduncle, and left frontal brain regions. One previously seen brain lesion had resolved. The Radiologist read the new MRI from the Rochester as typical for MS with no mention of Lyme disease. The spinal fluid analysis shows strong evidence for MS with positive oligoclonal bands, increase in immunoglobulin index and immunoglobulin synthesis. Protein was moderately high at 75 mg/dl and white cells were normal at 4. Spinal fluid was analyzed by PCR, a very sensitive way to detect the actual genetic material of the Lyme bacteria. PCR was negative (normal). The ID consultant stated that the positive screening (ELISA) tests were false positives and the WB Lyme tests confirmed that there was no evidence of Lyme disease. Repeat blood testing was also negative for Lyme. The ophthalmologist felt he had dry eyes and noted prior optic nerve damage, cause unknown. He agreed the MRI showed demyelinating (MS) lesions. He felt the lack of pain with the attacks was atypical for optic neuritis, however my review of the record does reflect Mr. Fix reported pain in December with his second attack.

Despite the conclusion that he did not have Lyme Disease and did have MS by the FMC and Mayo Clinic Neurologists and Infectious Disease specialists, Mr. Fix remained unconvinced. He remained at the FMC Rochester until his incarceration ended September 2001. He refused to accept his diagnosis of MS.

His next medical record available to me was from laboratory studies of 12/8/01, ordered by Dr. Joseph T. Joseph. These labs are normal showing signs of prior infection with Epstein Barr Virus and a minimal increase in his Sed Rate, a nonspecific finding. Dr. Joseph did not perform Lyme testing when he saw the patient on 12/19. Dr. Joseph's record states that the patient was bitten by a tick, had two bull's eye (target) rashes and that he had a history of tests that were positive for Lyme Disease. This data conflicts with the previous contemporaneous and more recent medical record as well as with documentation of what the patient was told. Over the following 2 years and 4 months Mr. Fix was treated with at least 14 different courses of antibiotics. Repeat blood tests were done on many occasions by Dr Joseph, however Dr. Joseph never obtained

independent testing for Lyme disease and consultation with a board certified Infectious Disease specialist, as should occur when a physician believes a patient has a serious or refractory infection.

Neurologist Dr Steven Shymansky evaluated Mr. Fix on 9/19/02. He confirmed a diagnosis of MS but was initially unsure regarding the possibility of Lyme Disease. Dr. Joseph's note of 10/3 has incorrect assumptions in it regarding Dr. Shymansky's impression. A repeat MRI Brain was done on 9/24, showing increased amount and distribution of lesions since the 5/25/01 scan. The 10/15/02 repeat Lyme screen IgM was positive however the repeat WB IgG was again negative. I agree with Dr. Shymansky's notation that the screening test is a false positive and that the patient does not have Lyme disease. I also agree with Dr. Shymansky that Dr. Joseph's antibiotic therapy was "quite excessive". Dr. Shymansky also suggested Mr. Fix go on Avonex to help control his MS. Dr. Joseph wrote a note to Mr. Fix on the date of his 11/9 office visit incorrectly stating that the 10/15 Lyme WB test was positive. On 1/03 Dr. Joseph placed Mr. Fix on intravenous antibiotic (Rocephin) therapy for weeks. A new MRI Brain scan was obtained on 2/24/03 and was read as showing increased number and prominence of lesions compared to 9/02. I agree with this comment and also note that brain atrophy has also increased. The MRI and MRI worsening are typical for MS. It has worsened since the patient received both the 8 week oral antibiotic treatment course and numerous oral and IV antibiotics through Dr. Joseph.

I have reviewed the literature regarding the diagnosis of Lyme Disease and am experienced at evaluating patients for possible Lyme Disease. Current standards set by experts in Lyme Disease and endorsed by the Centers for Disease Control (CDC) suggest that the laboratory testing for Lyme disease be a two step procedure. The first test is a screening test (often an ELISA or IFA). If this is positive, a Western Blot test is then performed as the screening test has too many false positives. (Reference MMWR 1995: 44:590-1). The American Academy of Neurology supports the use of these defined standards in making a diagnosis of Lyme Disease (AAN Practice Parameter, Neurology 1996; 46: 619-627), as does the family physician literature (American Family Physician 2005 (72): 297-304,309). Mr. Fix is an example of a patient who tests false positive. False positives occur as proteins similar to those detected in Lyme disease may occur spontaneously or with other infections. While few tests are 100% accurate, the most accurate testing available shows that Mr. Fix did not have infection with the Lyme bacteria on any of the dates tested. His initial and later symptoms are entirely consistent with MS and he did not experience other findings or symptoms in a way that would cause a prudent compassionate physician to treat as Lyme Disease. Dr. Joseph's assertion that the patient has Lyme disease is dubious. He is ignoring established medical standards in both his diagnosis and treatment of Mr. Fix.

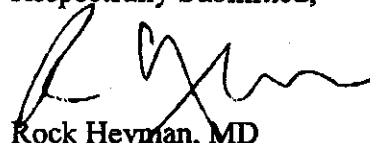
This patient meets all former and current diagnostic criteria for MS including the Schumacher Criteria, Poser Criteria, and both original and revised International Panel (McDonald) Criteria. I am highly experienced in applying these criteria, as they are vital to the correct classification of patients for clinical trials of investigational MS therapies. I am an investigator in such studies. I serve on the National Multiple Sclerosis Society's (NMSS) Medical Advisory Board, the NMSS National Council of Clinical Advisory Chairman, and am Chairman of the Education Committee of the Consortium of MS Centers.

Lyme infection of the nervous system usually will manifest as meningitis, meningoencephalitis, or cranial nerve palsies, or radiculomyelitis, or encephalopathy. While the optic nerve is a cranial nerve, it is among the least likely to be involved (see reference Coyle PK, Curr Neurol Neurosci Rep 2002 2(6): 479-87). Previous observations regarding positive Lyme testing in patients with optic neuritis (Jacobson et al, Neurology 1991 (5): 706-711 have been revised by the same author (Jacobson Neurology 2003 (60): 881) as routine screening for Lyme disease even in patients who reside in endemic areas is no longer recommended unless they have other typical symptoms of Lyme such as erythema migrans, fever, and joint pain. If testing is done, the above two-step protocol is recommended. There is insufficient evidence to support a causal link between Lyme disease and optic neuritis according to a thorough review of Lyme serology and optic neuritis (Silboni et al, J Neuro-Ophthalmology 2005 (25): 71-82.

The changes on the patient's MRI scans are highly typical for MS and continue to worsen despite the numerous treatments he has received for his erroneous diagnosis of Lyme disease. The intermittent resolution of some lesions is typical for MS. Standard treatment of Lyme disease may result in a marked resolution of MRI lesions (see Steinbach et al, Neurology 2005 (64): 758-759).

It is my medical opinion, based upon review of Mr. Fix's medical records and scans, that Mr. Fix has definite Multiple Sclerosis, that MS is the cause of his visual loss and neurologic abnormalities, and that there is no evidence that he has ever had Lyme disease involving his nervous system or eyes. I state these opinions are within a strong degree of medical certainty. I am an expert physician in the area of MS and an experienced physician in the evaluation of patients with suspected infectious or inflammatory diseases of the nervous system. My opinions regarding his diagnosis of MS and that MS are consistent with every neurologist's opinion who has personally evaluated him.

Respectfully Submitted,



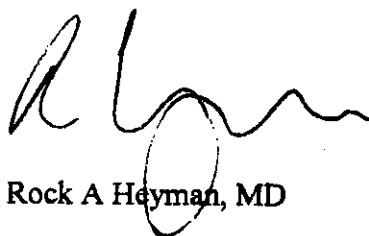
Rock Heyman, MD
Assistant Professor, Neurology
Chief, Division of Neuroimmunology and MS
University of Pittsburgh
Director, UPMC MS Center

ADDENDUM 10/13/06

Additional records from Dr DiMarco, Dr Felder, and Dr Joesph. I have reviewed the new MRI Brain films of March 28, 2006 and not the continued presence of lesions classic for MS on my review (as well as in the independent radiologist's report). I have reviewed the new spinal fluid analysis of 5/23/2006 which shows a mild protein elevation and the presence of oligoclonal bands, characteristic findings of MS. The continued presence of oligoclonal bands also argues against a previously treated infection being the

cause of Mr. Fix's prior optic neuritis and brain lesions as inflammation and antibody production (oligoclonal bands) would not continue unless infection continued. Repeat studies for Lyme disease were again negative in the spinal fluid as well. The assertion that a physician should diagnose Lyme disease involving the optic nerves or brain in the absence of serologic evidence to support infection is not correct by standards of neurologic, ophthalmologic, or infectious disease care. The physicians who continue to state that the patient's Lyme testing was positive are either not reviewing original diagnostic testing reports, not correctly interpreting the screening ELISA/IFA and confirmatory WB testing, or willing to diagnose any patient with a previous rash or skin lesion and any of a huge number of symptoms. To presume that a Lyme infection occurred (despite blood tests to the contrary), caused an at best extremely rare manifestation of Lyme disease (optic neuritis not only once but twice), and is the cause of Mr. Fix's disability is not logical when all clinical diagnostic criteria of MS are present, classic MRI findings are present (with new lesions showing up after antibiotic therapy), and persisting spinal fluid changes for MS are present.

My above opinions are strongly reinforced by the new MRI and spinal fluid data.



Rock A Heyman, MD